RECEIVED
CENTRAL FAX CENTER
JAN 24 2007

REMARKS

On January 21, 2007 the undersigned attorney spoke to Supervisory Examiner Dr. Tom McKenzie on January 23, 2007 regarding the following events:

On November 21, 2006, the undersigned attorney fax to Examiner R.J. Balls an Amendment responding to an Office Action setting forth a shortened statutory period for response ending January 27, 2007. After noting that the Amendment was not entered into the PAIR system, the undersigned attorney tried to contact Examiner Balls. After several unsuccessful attempts, the undersigned attorney called and spoke to Supervisory Examiner Dr. Tom McKenzie on January 23 to discuss how best to proceed. Given that we were still within the shortened statutory period for response, Examiner McKenzie, recommended sending the amendment anew. Applicants comply hereunder.

Claims 3, 4, 6-10, 19, 29-31 and 37-40 are pending in this application. Claims 3, 4, 6-10, 19, 29-31 were rejected solely on the ground of non-statutory obviousness-type double patenting.

At the middle of page 2 of the Action, the Examiner rejected claims 3, 4, 6-10, 19, 29-31 on the grounds of non-statutory double patenting obviousness over claim 20 (sic.) of co-pending application USSN 10/534,582. [Note that the species in question are the 12th and 18th species in claim 21 (not claim 20) of the co-pending '582 application.]

On November 15, 2006, the undersigned attorney spoke to Examiner Balls to confirm applicants understanding of the Office Action to the effect that cancellation of the species in question in the co-pending '582 application would resolve the issue. In addition, it was agreed that the species in question could be added to the instant application. These species are the subject of new claims 37-40. Applicants, point out that new claim 37 to 40 add no new matter. The species in question are found in the original claims, as filed. Applicants also direct the Examiner's attention to Examples 12 and 18. Regarding the phrase "or a pharmaceutically acceptable salt thereof", support is found, for example, in original claims 1 and 2 and at pages 15-16.

As will be seen in the attached copy of the Third Preliminary Amendment to co-pending application '582, applicants have canceled the species in question.

Having addresses all of the outstanding objections and rejection, applicants respectfully submit that the application is now in condition for allowance, and passage thereto is earnestly requested. The Examiner is invited to contact the undersigned attorney at the telephone number provided below if such would advance the prosecution of this case.

Respectfully submitted,

By Curtis C Panzer

Curtis C. Panzer
Reg. No. 33,752
Attorney for Applicant

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(908) 594-3199

Date: January 24, 2007

COPY

P&T OFFICE ACKNOWLEDGEMENT

ATTORNEY	DATE
Curtis C. Panzer	11/21/2006
CASE NUMBER	SERIAL NUMBER
MC073YP	10/534,582
DATE FILED	
May 11, 2005	
APPLICANT	
D. Dube, et al	
EXPRESS MAIL NO.	

The Patent & Trademark Office acknowledges, and has stamped hereon, the date of the receipt of the items checked below:

- ☒ AMENDMENT Third Preliminary
- ☐ APPEAL AND FEE
- ☐ ASSIGNMENT
- ☐ BRIEF
- ☐ CERTIFICATE OF CORRECTION
- ☐ FINAL FEE
- ☐ LETTER
- ☐ REQUEST FOR F.F. LICENSE
- ☐ INFORMATION DISCLOSURE STATEMENT
- ☐ PTO 1449 & REFERENCES
- ☐ PETITION FOR EXTENSION OF TIME & FEE
- ☐ INVITATION TO CORRECT
- ☐ DEMAND-CHAPTER II & FEE SHEET

F442<

PATENT
CASE NO. MC073YP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In re application of: D. DUBE, ET AL
Serial No. 10/534,582
Filed May 11, 2005
Group Art Unit 1625
Examiner R. Balls
For: 4-OXO-1-(3-SUBSTITUTED PHENYL-1,4-DIHYDRO-1,8-NAPHTHYRIDINE-3-CARBOXAMIDE PHOSPHODIESTERASE-4 INHIBITORS

Transmitted herewith is an amendment in the above-identified application.

☒ No additional fee is required.

☐ The fee has been calculated as shown below.

CLAIMS AS AMENDED

(1)	(2) Claims remaining after amendment	(3)	(4) Highest Number Previously Paid For	(5) Present Extra	(6) Rate	(7) Additional Fee
Total Claims	*	-	** 20 =	0 X	$50	= 0.00
Independent Claims	*	-	*** 3 =	0 X	$200	= 0.00
Multiple Dependent Claims					$360 ****	=
			TOTAL ADDITIONAL FEE FOR THIS AMENDMENT			0.00

* If the entry in Column 2 is less than the entry in Column 4, write "0" in Column 5.
** If the "Highest Number Previously Paid For" in this space is less than 20, write "20" in this space.
*** If the "Highest Number Previously Paid For" in this space is less than 3, write "3" in this space.
**** Add this fee only if application is amended to include multiple dependent claims (regardless of number) and no multiple dependent claims were originally filed.

Charge $ 0.00 to Deposit Account No. 13-2755. Please charge any additional fees or credit overpayment to Deposit Account No. 13-2755. A duplicate copy of this sheet is enclosed.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK & CO., INC.
By [signature] Date 21-NOV-2006

Respectfully,

[signature]

By: Curtis C. Panzer
Attorney for Applicant(s)
Reg. No. 33,752

MERCK & CO., INC.
Patent Dept., RY60-30
P.O. Box 2000
Rahway, N.J. 07065-0907

(732) 594-3199

IN DUPLICATE

PATENT
CASE NO. MC073YP

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

In re application of: D. DUBE, ET AL
Serial No. 10/534,582
Filed May 11, 2005
Group Art Unit 1625
Examiner R. Balls
For: 4-OXO-1-(3-SUBSTITUTED PHENYL-1,4-DIHYDRO-1,8-NAPHTHYRIDINE-3-CARBOXAMIDE PHOSPHODIESTERASE-4 INHIBITORS

Transmitted herewith is an amendment in the above-identified application.

☒ No additional fee is required.

☐ The fee has been calculated as shown below.

CLAIMS AS AMENDED

(1)	(2) Claims remaining after amendment	(3)	(4) Highest Number Previously Paid For	(5) Present Extra	(6) Rate	(7) Additional Fee
Total Claims	*	-	** 20 =	0 X	$50	= 0.00
Independent Claims	*	-	*** 3 =	0 X	$200	= 0.00
Multiple Dependent Claims					$360 ****	=
			TOTAL ADDITIONAL FEE FOR THIS AMENDMENT			0.00

* If the entry in Column 2 is less than the entry in Column 4, write "0" in Column 5.
** If the "Highest Number Previously Paid For" in this space is less than 20, write "20" in this space.
*** If the "Highest Number Previously Paid For" in this space is less than 3, write "3" in this space.
**** Add this fee only if application is amended to include multiple dependent claims (regardless of number) and no multiple dependent claims were originally filed.

Charge $ 0.00 to Deposit Account No. 13-2755. Please charge any additional fees or credit overpayment to Deposit Account No. 13-2755. A duplicate copy of this sheet is enclosed.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK & CO., INC.
By [signature] Date 21-NOV-2006

Respectfully,

[signature]

By: Curtis C. Panzer
Attorney for Applicant(s)
Reg. No. 33,752

MERCK & CO., INC.
Patent Dept., RY60-30
P.O. Box 2000
Rahway, N.J. 07065-0907

(732) 594-3199

RECEIVED
CENTRAL FAX CENTER
JAN 24 2007

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant :	D. Dube, et al.		
Serial No. :	10/534,582	Case MCO73YP	Art Unit: 1625
Filed :	May 11, 2005		Examiner: Balls, R.
For :	4-OXO-1-(3-SUBSTITUTED PHENYL-1,4-DIHYDRO-1,8-NAPHTHYRIDINE-3-CARBOXAMIDE PHOSPHODIESTERASE-4 INHIBITORS		

Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

THIRD PRELIMINARY AMENDMENT

Dear Sir:

Prior to examination in the merits please amend the above captioned application as indicated below. Any additional fees associated with this Amendment may be charged to Merck Deposit Account No. 13-2755.

AMENDMENTS TO THE CLAIMS are reflected in the listing of claims which begins on page 2 of this paper.

REMARKS begin on page 10 of this paper.

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date appearing below.

MERCK & CO., INC.

By _____ Date 21-Nov-2006

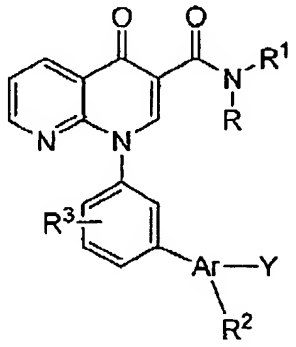
RECEIVED
CENTRAL FAX CENTER
JAN 24 2007

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listing of claims in the application.

1. (Canceled)

2. (Previously amended) A compound represented by Formula (I):



(I)

or a pharmaceutically acceptable salt thereof, wherein

Ar is phenyl, pyridyl, pyrimidyl, indolyl, quinolinyl, thienyl, pyridonyl, oxazolyl, oxadiazolyl, thiadiazolyl, or imidazolyl; or oxides thereof when Ar is a heteroaryl;

Y is –COOH, or -C_{1-6}alkyl(C_{1-4}alkyl)$_n$-COOH, wherein the -C_{1-6}alkyl is optionally substituted with halogen, alkoxy, hydroxy or nitrile, and the (C_{1-4}alkyl) substituents are optionally linked to form a C_{3-4}cycloalkyl ; wherein n is 0, 1, 2, 3 or 4;

R is H or –C_{1-6}alkyl;

R^1 is H, or –C_{1-6}alkyl, –C_{3-6}cycloalkyl, –C_{1-6}alkoxy, –C_{2-6}alkenyl, –C_{3-6}alkynyl, heteroaryl, or heterocycle group, optionally substituted with 1-3 independent haloC_{1-6}alkyl, -C_{1-6}alkyl, –C_{1-6}alkoxy, OH, amino, –(C_{0-6}alkyl)–SO_p–(C_{1-6}alkyl), nitro, CN, =N-O-C_{1-6}alkyl, -O-N=C_{1-6}alkyl, or halogen substituents, wherein p is 0, 1 or 2;

R^2 is H, halogen,-CN, -NO_2, –C_{1-6}alkyl, –C_{3-6}cycloalkyl, -O- C_{3-6}cycloalkyl, O-C_{1-6}alkyl, O-C_{3-6}cycloalkyl-C_{1-6}alkyl(C_{3-6}cycloalkyl)(C_{3-6}cycloalkyl), –C_{1-6}alkoxy, phenyl, heteroaryl, heterocycle, amino, –C(O)–C_{1-6}alkyl, –C(O)–O–C_{1-6}alkyl, –C_{1-6}alkyl(=N-OH), -C(N=NOH)C_{1-6}alkyl, –C_{0-6}alkyl(oxy)C_{1-6}alkyl-phenyl, –$SO_kNH(C_{0-6}$alkyl), or -(C_{0-6}alkyl)–SO_k–(C_{1-6}alkyl), wherein the phenyl, heteroaryl or heterocycle is optionally substituted with halogen, -C_{1-6}alkyl, –C_{1-6}alkoxy, hydroxy, amino,

or -C(O)-O-C_{1-6}alkyl, and wherein the alkyl or cycloalkyl is optionally substituted with 1-6 independently selected halogens or –OH, and wherein k is 0, 1, or 2;

R^3 is selected from H, halogen, CN, -C_{1-6}alkyl, -C_{3-6}cycloalkyl, nitro, -C(O)-C_{1-6}alkyl, -C(O)-O-C_{0-6}alkyl, -$SO_{n'}$NH(C_{0-6}alkyl), or -(C_{0-6}alkyl)-$SO_{n'}$-(C_{1-6}alkyl), O-C_{1-6}alkyl, O-C_{3-6}cycloalkyl, wherein n' is 0, 1, or 2 and wherein the alkyl and cycloalkyl is optionally substituted with 1-6 independently selected halogen or OH.

3 to 10. (Canceled)

11. (Original) The compound according to claim 2, or a pharmaceutically acceptable salt, wherein

Ar is pyridyl, pyrimidyl, or oxide thereof.

12. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt, wherein

R^1 is –C_{1-6}alkyl optionally substituted with 1-3 independent -C_{1-6}alkyl, –C_{1-6}alkoxy, OH, amino, –(C_{0-6}alkyl)–SO_p–(C_{1-6}alkyl), nitro, CN, =N-O-C_{1-6}alkyl, -O-N=C_{1-6}alkyl, or halogen substituents.

13. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R^1 is –C_{3-6}cycloalkyl optionally substituted with 1-3 independent -C_{1-6}alkyl, –C_{1-6}alkoxy, OH, amino, –(C_{0-6}alkyl)–SO_p–(C_{1-6}alkyl), nitro, CN, =N-O-C_{1-6}alkyl, -O-N=C_{1-6}alkyl, or halogen substituents.

14. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R is hydrogen.

15. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R^2 is hydrogen or .–C_{1-3}alkyl or halogen.

16. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R^1 is –C_{3-6}cycloalkyl optionally substituted with methyl or halo; and

R is hydrogen.

17. (Original) The compound according to claim 11, or a pharmaceutically acceptable salt thereof, wherein

R^1 is cyclopropyl optionally substituted with methyl or halo; and

R and R^2 are hydrogen or halogen;

R^3 is hydrogen or halogen.

18. (Original) The compound according to claim 2, or a pharmaceutically acceptable salt thereof, wherein

R and R^3 are hydrogen,;

R^1 is $-C_{3-6}$cycloalkyl optionally substituted with methyl or halo, or $-C_{1-3}$alkyl optionally substituted with 1-3 halo; and

Ar is phenyl.

19. (Canceled)

20. (Currently Amended) The compound which is

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;

2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}-2-methylpropanoic acid;

2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2-methylpropanoic acid;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-3-methylbutanoic acid;

{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}(hydroxy)acetic acid;

1-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(cis)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

5-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2,2-dimethyl-1,3-dioxolane-4-carboxylic acid;

1-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;

1-cyano-3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-2,2-dimethylcyclopropanecarboxylic acid;

~~2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-fluoro-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;~~

(cis)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-3-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-bromo-5'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-methyl-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-2-methyl-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3-chloro-3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

~~2-(cis)-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-3-fluoro-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;~~

3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-carboxylic acid;

2-(trans)-{3'-[3-(morpholin-4-ylcarbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[4-oxo-3-({[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]amino}carbonyl)-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-({[2-(methylthio)ethyl]amino}carbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[3-({[2-(methylsulfonyl)ethyl]amino}carbonyl)-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;

2-(trans)-(5-{3-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]phenyl}thien-2-yl)cyclopropanecarboxylic acid;
2-(trans)-{3'-[3-{[(cyclopropylmethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid;
2-(trans)-{3'-[3-{[(1-cyanocyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}cyclopropanecarboxylic acid; or
3-{3'-[3-[(isopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-1,1'-biphenyl-4-yl}-3-methylbutanoic acid, or a pharmaceutically acceptable salt thereof.

21. (Currently amended) A The compound which is

(+)-(trans)-2-{3-fluoro-3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}methyl)cyclobutanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2-methylcyclopropanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}cyclopropanecarboxylic acid;
3-methyl-3-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}butanoic acid;
(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}cyclopropanecarboxylic acid;
(trans)-2-{3'-[4-oxo-3-{[(2,2,3,3,3-pentafluoropropyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
(trans)-2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-1-fluorocyclopropanecarboxylic acid;
(+)-(trans)-2-{3-chloro-3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;
(-)-(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-ethyl 2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylate;

(+)-(trans)-isopropyl 2-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylate;

tert-butyl 3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2,2-dimethylpropanoate;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2,2-dimethylpropanoic acid;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-3-yl}-2,2-dimethylpropanoic acid;

1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-3-yl}methyl)cyclobutanecarboxylic acid;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}-2,2-dimethylpropanoic acid;

1-({3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-2-yl}methyl)cyclobutanecarboxylic acid;

(+)-(trans)-2-{3'-[3-[(*tert*-butylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[3-[(cyclobutylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

3-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}bicyclo[1.1.1]pentane-1-carboxylic acid;

4-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-4-hydroxypentanoic acid;

~~(trans)-2-{3'-[3-{[(□)-cis-(2-fluorocyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;~~

(trans)-2-{3'-[3-{[(±)-cis-(2-fluorocyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[3-{[(dicyclopropylmethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

4-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-2,2-dimethylbutanoic acid;

(+)-(trans)-2-{3'-[3-{[(1-hydroxycyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[4-oxo-3-{[(1-phenylcyclopropyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

4-{3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}-3,3-dimethylbutanoic acid;

(+)-(trans)-2-{3'-[3-{[(1-cyclopropyl-1-methylethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

1-({3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}methyl)cyclobutanecarboxylic acid;

(+)-(trans)-2-{3'-[3-{[(cyclopropylmethyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

(-)-(trans)-2-{3-fluoro-3'-[3-{[(1-hydroxycyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

~~(trans)-2-{3'-[4-oxo-3-{[((□)-2,2,2-trifluoro-1-methylethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;~~

(trans)-2-{3'-[4-oxo-3-{[((±)-2,2,2-trifluoro-1-methylethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]-(+)-biphenyl-4-yl}cyclopropanecarboxylic acid;

(+)-(trans)-2-{3'-[3-{[(1-methylcyclopropyl)amino]carbonyl}-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid;

2,2-dimethyl-4-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}butanoic acid;

2,2-dimethyl-3-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}propanoic acid;

(-)-(trans)-2-{3-chloro-3'-[3-[(cyclopropylamino)carbonyl]-4-oxo-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid; or

(+)-(trans)-2-{3'-[4-oxo-3-{[(2,2,2-trifluoroethyl)amino]carbonyl}-1,8-naphthyridin-1(4*H*)-yl]biphenyl-4-yl}cyclopropanecarboxylic acid, or a pharmaceutically acceptable salt thereof.

22. (Previuosly amended) A pharmaceutical composition comprising

a therapeutically effective amount of the compound according to claim 2 or a pharmaceutically acceptable salt thereof; and

a pharmaceutically acceptable carrier.

23 to 24. (Canceled).

25. (Previuosly amended) A method of treatment or prevention of asthma, chronic bronchitis, chronic obstructive pulmonary disease (COPD), eosinophilic granuloma, psoriasis and other benign or malignant proliferative skin diseases, endotoxic shock (and associated conditions such as laminitis and colic in horses), septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, inflammatory arthritis, osteoporosis, chronic glomerulonephritis, atopic dermatitis, urticaria, adult respiratory distress syndrome, infant respiratory distress syndrome, chronic obstructive pulmonary disease in animals, diabetes insipidus, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, arterial restenosis, atherosclerosis, neurogenic inflammation, pain, cough, rheumatoid arthritis, ankylosing spondylitis, transplant rejection and graft versus host disease, hypersecretion of gastric acid, bacterial, fungal or viral induced sepsis or septic shock, inflammation and cytokine-mediated chronic tissue degeneration, osteoarthritis, cancer, cachexia, muscle wasting, depression, memory impairment, monopolar depression, acute and chronic neurodegenerative disorders with inflammatory components, Parkinson disease, Alzheimer's disease, spinal cord trauma, head injury, multiple sclerosis, tumour growth and cancerous invasion of normal tissues comprising the step of administering a therapeutically effective amount, or a prophylactically effective amount, of the compound according to claim 2 or a pharmaceutically acceptable salt thereof.

26. (Previuosly amended) A method of enhancing cognition in a healthy subject comprising administering a safe cognition enhancing amount of compound according to claim 2, or a parmaceutically salt thereof.

27 to 34. (Canceled)

RECEIVED
CENTRAL FAX CENTER
JAN 24 2007

REMARKS

Claims 2, 11-18, 20-22, 25 and 26 are pending in this application.

In co-pending application 10/764,229, Applicants received an Office Action dated October 27, 2006 indicating that the claims therein were rejected as representing obviousness type double patenting over the instant application. In particular, the Examiner noted that the 12 and 18 species of claim 20 (sic.) of the instant application were the cis and trans species of the compound of claim 30 in co-pending '229. [Note that the species in question are in claim 21, not 20] To remove this issue, applicants have canceled the species in question in the instant application and added them to co-pending '229.

Observe that applicants have made futher amendments to claim 21. In particular, they have added "or a pharmaecutically acceptable salt thereof" to the end of the claim. Applicants have also corrected the names of the 6th and 16th species from the end of the claim to match that of Example 61, found at page 86 and Example 51, found at page 85. Applicants respectfully submit that these amendments do not add new matter. Regarding "or a pharmaecutically acceptable salt thereof", support is found, for example, in original claims 1 and 2 and at pages 15 and 16 of the specification. As mentioned above, the correct names of the species are found in Examples 61 and 51.

Observe also, that "or a pharmaecutically acceptable salt thereof" has been added to claim 20. For the reasons mentioned above this amendment adds no new matter. Finally, applicants direct the Examiner's attention to the fact that in their "Second Preliminary Amendment", they correctly show an amendment to claim 20 (i.e. removing a dependency) but incorrectly styled the claim as "(Original)" rather than "(Currently amended)".

U.S.S.N.
CASE NO. MCO73YP
PAGE NO. 11

Applicants respectfully request early examination of this application. The Examiner is invited to contact the undersigned attorney at the telephone nuber provided below, if such would advance the prosecution of this application.

Respectfully submitted,

By _____
Curtis C. Panzer
Reg. No. 33,752
Attorney for Applicant

MERCK & CO., Inc.
P.O. Box 2000
Rahway, New Jersey 07065-0907
(732) 594-3199

Date: November 21, 2006